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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/912,717	07/24/2001	Jennifer L. Hillman	PF-0532-2 DIV	5873

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INCYTE GENOMICS, INC.
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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	9

DATE MAILED: 09/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/912,717	Applicant(s) HILLMAN ET AL.	
	Examiner " Neon" Phuong Huynh	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-63* is/are pending in the application.

4a) Of the above claim(s) *48,51,53,62 and 63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-47, 49-50, 52 and 54-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 45-63 are pending.

2. Newly submitted claims 48, 51, 53 and 62-63 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claim 48 is drawn a diagnostic test, which is a product. Claims 51 and 53 are drawn to a method of diagnosing a condition or disease using antibody, while claim 62 is drawn to a method of detecting a polypeptide and claim 63 is drawn to a method of purifying a polypeptide using antibody. Inventions of Newly submitted claims 51, 53, 62-63 are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the methods of purifying versus the methods of diagnosing and detecting a polypeptide differ with their respect to their process steps and endpoints. Therefore, they are patentably distinct. Inventions of Claim 48 and Claims 51, 53 and 62-63 are unrelated. Claim 48 is drawn a diagnostic test, which is a product while claims 51, 53 and 62-63 are drawn to various methods which drawn to different class and subclass. A search of one group will not encompass the other. Inventions of claim 48 and claims 45-47, 49-50, 52 and 54-61 are distinct products. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the products a diagnostic kit versus antibody as claimed differ with respect to structure and physiochemical properties. Therefore, they are patentably distinct.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 48, 51, 53 and 62-63 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. Claims 45-47, 49-50, 52 and 54-61 are being acted upon.

4. The Double Patenting rejection of claims 28, 31, 33 and 35-40 is hereby withdrawn in view of the terminal disclaimer under 37 CFR 1.321 filed 6/24/02 by Richard C. Ekstrom.

5. In view of the amendment filed 6/24/02, the following rejections remain.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 45-47, 49-50, 52 and 54-61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) an isolated antibody which specifically binds to a purified polypeptide comprising an amino acid sequence of SEQ ID NO: 1; (2) the antibody mentioned above wherein the antibody is a chimeric, single chain. Fab fragment, F(ab')2 fragment or humanized antibody, (3) a composition comprising an isolated antibody which specifically binds to a purified polypeptide comprising an amino acid sequence of SEQ ID NO: 1 and an acceptable excipient, (4) a composition comprising an isolated antibody which specifically binds to a purified polypeptide comprising an amino acid sequence of SEQ ID NO: 1 and an acceptable excipient wherein the antibody is labeled, (5) a method of preparing a polyclonal antibody with the specificity of an isolated antibody which specifically binds to a purified polypeptide comprising an amino acid sequence of SEQ ID NO: 1 comprising a) immunizing an animal with a polypeptide having the amino acid sequence of SEQ ID NO: 1 or an immunogenic fragment thereof, under the conditions to elicit an antibody response; b) isolating antibodies from said animal and c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal antibody which binds specifically to a polypeptide having the amino acid sequence of SEQ IDNO: 1; (6) a polyclonal antibody produced by a method of preparing a polyclonal antibody with the specificity of an isolated antibody which specifically binds to a purified polypeptide comprising an amino acid sequence of SEQ ID NO: 1 comprising a) immunizing an animal with a polypeptide having the amino acid sequence of SEQ ID NO: 1 or an immunogenic fragment thereof, under the conditions to elicit an antibody response; b) isolating antibodies from said animal and c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal antibody which binds specifically to a polypeptide having the amino acid sequence of SEQ IDNO: 1; (7) a composition comprising the polyclonal antibody mentioned above and a suitable carrier, (8) a method of making a monoclonal antibody with the specificity of the antibody that specifically binds to a purified polypeptide comprising an amino acid sequence of SEQ ID NO: 1, the method comprising: a) immunizing an animal with a polypeptide having the

amino acid sequence of SEQ ID NO: 1, under the conditions to elicit an antibody response, b) isolating antibody producing cells from the animal; c) fusing the antibody producing cells with immortalized cells to form monoclonal antibody-producing hybridoma cells; d) culturing the hybridoma cells and e) isolating from the culture monoclonal antibody which binds specifically to a polypeptide consisting of amino acid sequence of SEQ ID NO: 1; (9) A monoclonal antibody produced by a) immunizing an animal with a polypeptide having the amino acid sequence of SEQ ID NO: 1 under the conditions to elicit an antibody response, b) isolating antibody producing cells from the animal; c) fusing the antibody producing cells with immortalized cells to form monoclonal antibody-producing hybridoma cells; d) culturing the hybridoma cells and e) isolating from the culture monoclonal antibody which binds specifically to a polypeptide consisting of amino acid sequence of SEQ ID NO: 1 and (10) An isolated antibody specifically binds to a purified polypeptide comprising an amino acid sequence of SEQ ID NO: 1 produced by screening a recombinant library or by screening a recombinant immunoglobulin library for diagnostic assays, **does not** reasonably provide enablement for (1) *any* isolated antibody which specifically binds to *any* polypeptide "comprising" a) *any* naturally-occurring amino acid sequence having at least 90% sequence identical to the amino acid sequence of SEQ ID NO: 1, said naturally occurring amino acid sequence having 1-pyrroline-5-carboxylate reductase activity, (2) the antibody which specifically binds to a polypeptide "comprising" any naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 1, said naturally occurring amino acid sequence having 1-pyrroline-5- carboxylate reductase activity, (3) the antibody which specifically binds to *any* polypeptide "comprising" a) *any* naturally-occurring amino acid sequence having at least 90% sequence identical to the amino acid sequence of SEQ ID NO: 1 wherein the antibody is a chimeric antibody, a single chain antibody, a Fab fragment, a F(ab')2 fragment or a humanized antibody, (4) a composition comprising an antibody which specifically binds to *any* polypeptide "comprising" a) *any* naturally-occurring amino acid sequence having at least 90% sequence identical to the amino acid sequence of SEQ ID NO: 1, said naturally occurring amino acid sequence having 1-pyrroline-5-carboxylate reductase activity and an acceptable excipient, (5) a composition comprising an antibody which specifically binds to *any* polypeptide "comprising" a) *any* naturally-occurring amino acid sequence having at least 90% sequence identical to the amino acid sequence of SEQ ID NO: 1, said naturally occurring amino acid sequence having 1-pyrroline-5-carboxylate reductase activity and an acceptable excipient wherein the antibody is labeled, (6) a method preparing a polyclonal or monoclonal

antibody with the specificity of the antibody of which specifically binds to *any* polypeptide "comprising" a) *any* naturally-occurring amino acid sequence having at least 90% sequence identical to the amino acid sequence of SEQ ID NO: 1, said naturally occurring amino acid sequence having 1-pyrroline-5-carboxylate reductase activity, the method comprising: a) immunizing an animal with a polypeptide having the amino acid sequence of SEQ ID NO: 1 or an immunogenic fragment thereof, under the conditions to elicit an antibody response; b) isolating antibodies from said animal and c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal antibody which binds specifically to a polypeptide having the amino acid sequence of SEQ IDNO: 1; (7) a polyclonal antibody produced by the method mentioned above, (8) a composition comprising the polyclonal antibody with the specificity of the antibody of which specifically binds to *any* polypeptide "comprising" a) *any* naturally-occurring amino acid sequence having at least 90% sequence identical to the amino acid sequence of SEQ ID NO: 1, said naturally occurring amino acid sequence having 1-pyrroline-5-carboxylate reductase activity, the method comprising: a) immunizing an animal with a polypeptide having the amino acid sequence of SEQ ID NO: 1 or an immunogenic fragment thereof, under the conditions to elicit an antibody response; b) isolating antibodies from said animal and c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal or antibody which binds specifically to a polypeptide having the amino acid sequence of SEQ IDNO: 1 and a suitable carrier, (9) any composition comprising said polyclonal antibody and an acceptable excipient, (10) A method of making *any* monoclonal antibody with the specificity of binding to *any* polypeptide "comprising" a) *any* naturally-occurring amino acid sequence having at least 90% sequence identical to the amino acid sequence of SEQ ID NO: 1, said naturally occurring amino acid sequence having 1-pyrroline-5-carboxylate reductase activity, the method comprising: a) immunizing an animal with a polypeptide having the amino acid sequence of SEQ ID NO: 1 or an immunogenic fragment thereof, under the conditions to elicit an antibody response; b) isolating antibodies from said animal; c) fusing the antibody producing cells with immortalized cells to form monoclonal antibody-producing hybridoma cells; d) culturing the hybridoma cells, and e) isolating from the culture monoclonal antibody which binds specifically to a polypeptide having the amino acid sequence of SEQ ID NO: 1, (11) *any* monoclonal antibody produced by the method mentioned above, (12) *any* composition comprising said monoclonal antibody and a suitable carrier, (13) *any* antibody which specifically binds to *any* polypeptide "comprising" a) *any* naturally-occurring amino acid sequence having at least 90% sequence identical to the amino

acid sequence of SEQ ID NO: 1, said naturally occurring amino acid sequence having 1-pyrroline-5-carboxylate reductase activity wherein the antibody is produced by screening a Fab expression library or recombinant immunoglobulin library for immunoaffinity chromatography. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only an isolated antibody which specifically binds to a polypeptide comprising an amino acid sequence of SEQ ID NO: 1 wherein the antibody is a chimeric antibody, a single chain antibody, a Fab fragment, a F(ab')2 fragment thereof or a humanized antibody and a method of producing said antibody for diagnostic and detection assays (See page 19, lines 26-34, pages 24-25, 44).

The specification does not teach how to make and use *any* antibody that binds to a polypeptide comprising any "naturally occurring" amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 1, much less said naturally occurring amino acid sequence having any 1-pyrroline-5-carboxylate reductase activity. The term "having" or "comprising" is open-ended. It expands the "naturally occurring" amino acid sequence to include additional amino acids at either or both ends. Given the indefinite number of undisclosed "naturally occurring" amino acid sequence where the sequence can reach infinity, there is insufficient guidance and working example as how the sequence can be 90% identical, much less having 1-pyrroline-5-carboxylate reductase activity. Even if the "naturally occurring" amino acid sequence has the same number of amino acids as the claimed sequence of SEQ ID NO: 1 (314 amino acids in length), a 90% identity means 10% difference, which translates to 31 amino acids difference.

Kuby *et al,* of record, teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimentional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the full-length polypeptide. Without the specific amino acid residues, it is unpredictable which undisclosed antibody such as polyclonal or monoclonal, chimeric, single chain, Fab fragment F(ab')2 fragment or humanized antibody generated from any undisclosed "naturally occurring" amino acid sequence and fragment thereof would bind specifically to a polypeptide comprising any naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 1. It is known that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site. Given the undisclosed antigenic determinant, it is also unpredictable which undisclosed antibody such as polyclonal or monoclonal, chimeric, single chain, Fab fragment F(ab')2 fragment or humanized antibody generated from immunizing an animal with a polypeptide having the amino acid sequence of SEQ ID NO: 1 or an "immunogenic fragment thereof" would binds specifically to SEQ ID NO: 1, much less binding to a polypeptide comprising any naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 1. Since the antibody is not enabled, it follows that any composition comprising said antibody is not enabled.

With regard to composition comprising any polyclonal or monoclonal antibody and an acceptable excipient or suitable carrier, the specification fails to provide any *in vivo* working examples, or guidance with respect to treating a patient suffering from *any* disease using *any* antibody mentioned above. Given the indefinite number of disease, the lack of guidance and in vivo working examples, further research is required. Since the composition comprising said antibody is not enabled, it follows that composition comprising the labeled antibody is not enabled.

The '370 patent, of record, teaches that the inherent problem with chimeric antibody has been a loss of affinity for the antigen, which means more antibody will have to be injected into a patient at higher cost and greater risk of adverse effects such as serum sickness (See column 2 lines 12-27, in particular). In the absence of in vivo working examples, it is unpredictable for the following reasons: (1) the antibody may be inactivated before producing an effect, i.e. such as inherently short half-life of the antibody; (2) the antibody may not reach the target area; and (3)

other functional properties, known or unknown, may make the antibody unsuitable for *in vivo* therapeutic use, i.e. such as serum sickness which prohibitive to the use of antibody for such treatment. Therefore, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 6/24/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) the specification teaches how to make and use antibodies including variants having 90% sequence identity to SEQ ID NO: 1 as well as fragment of SEQ ID NO: 1, (2) new claims include the functional language of "1-pyrroline-5-carboxylate reductase activity" and (3) the fragment language has been deleted from the claims.

However, there is no showing of any antibody ever made such as immunizing a rabbit or mice with polypeptide of SEQ ID NO: 1 or antigenic fragment thereof would generate antibody that binds specifically to a polypeptide comprising any "naturally occurring" amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 1.

8. Claims 45-47, 49-50, 52 and 54-61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* isolated antibody which specifically binds to *any* polypeptide "comprising" a) *any* naturally-occurring amino acid sequence having at least 90% sequence identical to the amino acid sequence of SEQ

ID NO: 1, said naturally occurring amino acid sequence having 1-pyrroline-5-carboxylate reductase activity, (2) the antibody which specifically binds to a polypeptide "comprising" any naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 1, said naturally occurring amino acid sequence having 1-pyrroline-5- carboxylate reductase activity, (3) the antibody which specifically binds to *any* polypeptide "comprising" a) *any* naturally-occurring amino acid sequence having at least 90% sequence identical to the amino acid sequence of SEQ ID NO: 1 wherein the antibody is a chimeric antibody, a single chain antibody, a Fab fragment, a F(ab')2 fragment or a humanized antibody, (4) a composition comprising an antibody which specifically binds to *any* polypeptide "comprising" a) *any* naturally-occurring amino acid sequence having at least 90% sequence identical to the amino acid sequence of SEQ ID NO: 1, said naturally occurring amino acid sequence having 1-pyrroline-5-carboxylate reductase activity and an acceptable excipient, (5) a composition comprising an antibody which specifically binds to *any* polypeptide "comprising" a) *any* naturally-occurring amino acid sequence having at least 90% sequence identical to the amino acid sequence of SEQ ID NO: 1, said naturally occurring amino acid sequence having 1-pyrroline-5-carboxylate reductase activity and an acceptable excipient wherein the antibody is labeled, (6) a method preparing a polyclonal or monoclonal antibody with the specificity of the antibody of which specifically binds to *any* polypeptide "comprising" a) *any* naturally-occurring amino acid sequence having at least 90% sequence identical to the amino acid sequence of SEQ ID NO: 1, said naturally occurring amino acid sequence having 1-pyrroline-5-carboxylate reductase activity, the method comprising: a) immunizing an animal with a polypeptide having the amino acid sequence of SEQ ID NO: 1 or an immunogenic fragment thereof, under the conditions to elicit an antibody response; b) isolating antibodies from said animal and c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal antibody which binds specifically to a polypeptide having the amino acid sequence of SEQ IDNO: 1; (7) a polyclonal antibody produced by the method mentioned above, (8) a composition comprising the polyclonal antibody with the specificity of the antibody of which specifically binds to *any* polypeptide "comprising" a) *any* naturally-occurring amino acid sequence having at least 90% sequence identical to the amino acid sequence of SEQ ID NO: 1, said naturally occurring amino acid sequence having 1-pyrroline-5-carboxylate reductase activity, the method comprising: a) immunizing an animal with a polypeptide having the amino acid sequence of SEQ ID NO: 1 or an immunogenic fragment thereof, under the conditions to elicit an antibody response; b) isolating

antibodies from said animal and c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal or antibody which binds specifically to a polypeptide having the amino acid sequence of SEQ IDNO: 1 and a suitable carrier, (9) any composition comprising said polyclonal antibody and an acceptable excipient, (10) A method of making *any* monoclonal antibody with the specificity of binding to *any* polypeptide "comprising" a) *any* naturally-occurring amino acid sequence having at least 90% sequence identical to the amino acid sequence of SEQ ID NO: 1, said naturally occurring amino acid sequence having 1-pyrroline-5-carboxylate reductase activity, the method comprising: a) immunizing an animal with a polypeptide having the amino acid sequence of SEQ ID NO: 1 or an immunogenic fragment thereof, under the conditions to elicit an antibody response; b) isolating antibodies from said animal; c) fusing the antibody producing cells with immortalized cells to form monoclonal antibody-producing hybridoma cells; d) culturing the hybridoma cells, and e) isolating from the culture monoclonal antibody which binds specifically to a polypeptide having the amino acid sequence of SEQ ID NO: 1, (11) *any* monoclonal antibody produced by the method mentioned above, (12) *any* composition comprising said monoclonal antibody and a suitable carrier, (13) *any* antibody which specifically binds to *any* polypeptide "comprising" a) *any* naturally-occurring amino acid sequence having at least 90% sequence identical to the amino acid sequence of SEQ ID NO: 1, said naturally occurring amino acid sequence having 1-pyrroline-5-carboxylate reductase activity wherein the antibody is produced by screening a Fab expression library or recombinant immunoglobulin library for immunoaffinity chromatography.

The specification discloses only an isolated antibody which specifically binds to a polypeptide comprising an amino acid sequence of SEQ ID NO: 1 wherein the antibody is a chimeric antibody, a single chain antibody, a Fab fragment, a F(ab')2 fragment thereof or a humanized antibody and a method of producing said antibody for diagnostic and detection assays (See page 19, lines 26-34, pages 24-25, 44).

With the exception of the specific antibody that binds to a polypeptide consisting of SEQ ID NO: 1, there is insufficient written description about the structure associated with function of an isolated antibody that binds to *any* polypeptide "naturally-occurring" amino acid sequence at least "90% sequence identity" to the amino acid sequence of SEQ ID NO: 1 for in vivo treatment of any disease and diagnostic assays. Since the polypeptide to which the antibody binds is only 90% identical to SEQ ID NO: 1, there is insufficient written description about the other 10%, much less about any other "naturally-occurring" polypeptide. Further, given the lack of a written

description of *any* additional representative species of polypeptide other than the polypeptide of SEQ ID NO: 1 to which the antibody binds wherein the antibody is polyclonal, monoclonal, chimeric, humanized, Fab fragment, F(ab')2 fragment thereof, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 6/24/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) new claim 45 includes functional language of "1-pyrroline-5-carboylate reductase activity" and the "fragment language" has been deleted.

However, there is insufficient written description about the structure associated with function of an isolated antibody that binds to *any* polypeptide "naturally-occurring" amino acid sequence at least "90% sequence identity" to the amino acid sequence of SEQ ID NO: 1 for in vivo treatment of any disease and diagnostic assays. Since the polypeptide to which the antibody binds is only 90% identical to SEQ ID NO: 1, there is insufficient written description about the other 10%, much less about any other "naturally-occurring" polypeptide. Further, given the lack of a written description of *any* additional representative species of polypeptide other than the polypeptide of SEQ ID NO: 1 to which the antibody binds wherein the antibody is polyclonal, monoclonal, chimeric, humanized, Fab fragment, F(ab')2 fragment thereof, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

9. No claim is allowed.

10. **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the

mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

12. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
September 30, 2002

Christina Chan
CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600